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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/645,794	08/21/2003	Andrew J. Bett	20699Y	8205
210	7590	06/29/2006	EXAMINER	
MERCK AND CO., INC P O BOX 2000 RAHWAY, NJ 07065-0907			HORNING, MICHELLE S	
			ART UNIT	PAPER NUMBER
			1648	

DATE MAILED: 06/29/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/645,794	BETT ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Michelle Horning	1648	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 4/03/2006.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-83 is/are pending in the application.
- 4a) Of the above claim(s) 12-20, 24-29, 31-44, 46-57, 59-72, 74-83 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-11, 21-23 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                        | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)               | Paper No(s)/Mail Date. _____  |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                                    |

### **DETAILED ACTION**

This application has been transferred to another examiner. Please direct any further correspondence regarding this application to Examiner Michelle Horning.

This office action is in response to the communication received 4/03/2006. The status of the claims is as follows: claims 1-83 are pending; claims 1-11 and 21-23 are under examination; claims 12-20, 24-29, 31-44, 46-57, 59-72 and 74-83 have been withdrawn; and claims 30, 45, 58 and 73 are drawn to a non-elected species.

The rejections under 35 U.S.C. § 112, Second Paragraph and 103 (a) from the previous office action have been withdrawn following the amendments of the claims and the opinion of the current examiner, respectively. In regards to the latter, the current examiner respectfully agrees with Applicant's response. This action is non-final.

### ***Claim Rejections - 35 USC § 112, 2***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-11 and 21-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 1-11 and 21-23 are drawn to a "means" and fail to distinctly describe what the "means" in the claims represent (e.g. an apparatus or a method).

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

*Claims 1-7 and 10 are rejected under 35 U.S.C. 102(e) as being anticipated by Mehtali et al, US Patent No. 6,475,780 (hereafter "Mehtali et al"). This rejection is maintained in response to applicant's response following the previous office action.*

Applicant argues that the vector used by Mehtali et al does not possess a heterologous E4. Furthermore, applicant states in the response that the adenovirus is "not grown in a complementing cell line expressing an E1 of distinct serotype from the adenovirus being propagated therein". Applicant further argues this point by stating that the Ad5 serotype vector are grown in 293 cells which express E1 derived from Ad5.

Applicant's arguments are considered but are found unpersuasive. Mehtali et al recite the use of a heterologous E4 throughout the patent. Supporting statements can

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be found in the following places: col. 4, lines 35-41, col. 7, lines 55-56 and col. 9, lines 35-38. Moreover, Mehtali et al also state the use of an Ad2 adenovirus as well as an Ad5 adenovirus found in claim 8. The use of an Ad2 adenovirus combined with 293 cells expressing E1 derived from Ad5 satisfies the limitation of distinct serotypes between the E1 and adenovirus claimed by Applicant. Based on this disclosure, Mehtali et al anticipate the subject matter of claims 1-7 and 10.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

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*Claims 21-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mehtali et al in view of Inglis et al, U.S. Patent No 5,665,362. This rejection is maintained in response to applicant's response following the previous office action.*

As noted above, Applicant argues that the vector used by Mehtali et al does not possess a heterologous E4. In addition, Applicant further argues that Mehtali et al uses an Ad5 serotype vector combined with 293 cells that express E1 derived from Ad5. This combination according to the Applicant does not satisfy the limitation of "distinct serotype" set forth in the Applicant's claims.

However, as previously mentioned, Mehtali et al recite the use of a heterologous E4 throughout the patent, including statements made in col. 4, lines 35-41, col. 7, lines 55-56 and col. 9, lines 35-38. Moreover, Mehtali et al also state the use of an Ad2 adenovirus as found in claim 8. Given that Mehtali et al teach all the limitations previously discussed, including expressly citing the method as a use for producing HIV antigenic polypeptide (col. 6, lines 41-44), and Inglis et al disclose a replication-defective adenovirus comprising a nucleotide encoding an HIV-1 gag antigen, this rejection is maintained.

### ***Claim Rejections - 35 USC § 103***

*Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Mehtali et al in view of Li et al, U.S. Patent No 7,026,164.*

Mehtali et al teach the method of using an adenoviral E4 reading frame to improve the expression of a gene of interest combined with an E1 complimenting cell

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line (entire document). Mehtali et al teach the use of cell line 293 (col. 10, lines 5-10).

Mehtali et al do not disclose the use or a working example of a PER.C6® cell line. Li et al disclose a packaging cell line, PER.C6® cell line, used for the production of recombinant adenoviral vectors and replication defective adenoviral vectors with E1 early gene region deletions (see abstract).

Therefore, it would have been obvious to one of ordinary skill in the art to use the PER.C6® cell line in the method taught by Mehtali et al. One would have been motivated to do so to reduce unwanted recombination events between the cell line and vector as suggested by Li et al (col. 2, 17-38). There would have been a reasonable expectation of success, given that the cell line was commonly used in the art to produce sufficient amounts of adenovirus. Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

### ***Claim Rejections - 35 USC § 103***

*Claims 8 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mehtali et al in view of Goossens et al.*

Mehtali et al teach the method of using an adenoviral E4 reading frame to improve the expression of a gene of interest combined with an E1 complimenting cell line (entire document). Mehtali et al teach the use of combining serotypes Ad5 and Ad2 (vector found in claim 8, cell line described in col. 10, lines 5-10). Mehtali et al do not teach the combination of serotypes Ad5 and Ad35 within a vector. Goossens et al overcomes this limitation by disclosing chimeric adenoviruses based on Ad5 but



carrying the DNA encoding adenovirus from subgroup B, including Ad11, Ad 16 and Ad 35. The chimeric vectors were produced in PER.C6® cells. (see abstract, under methods).

Therefore, it would have been obvious to one of ordinary skill in the art to modify the methods by Mehtali et al for the propagation of adenoviruses. One would have been motivated to do so because the data presented by Goossens et al teach that a chimeric vector comprised of Ad5 and Ad16 is far superior to Ad5 in transfecting cells, as measured by the amount of cells transduced and the amount of transgene expressed per a cell (page 575, 2<sup>nd</sup> paragraph of discussion). Goossens et al also teach that this is also true for a chimeric vector comprised of Ad5 and Ad35 (figure 2). There would have been a reasonable expectation of success to make a chimeric vector by standard molecular biology skills as taught by Goossen et al. Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

### CONCLUSION

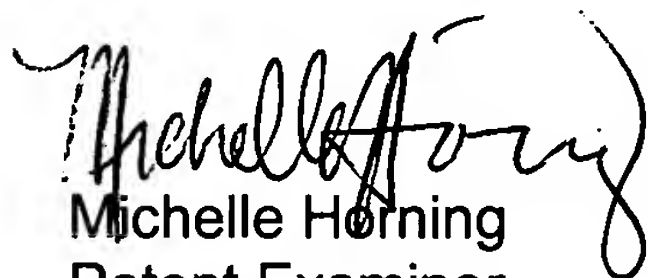
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michelle Horning whose telephone number is 571-272-9036. The examiner can normally be reached on Monday-Friday, 8:30 am to 5 pm.

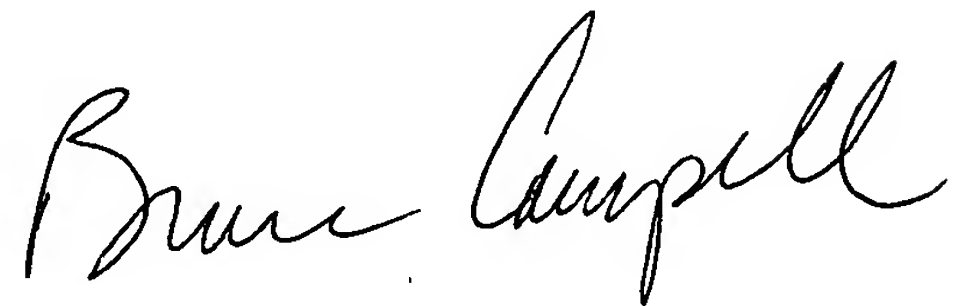
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 570-272-8300.



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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for unpublished application is available through Private PAIR only. For more information about PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
Michelle Horning  
Patent Examiner



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